

What is claimed is:

1. A method of predicting a behavior of a biochemical system, comprising:

(a) comparing two or more data integration maps 5 of a biochemical system obtained under different conditions, said data integration map comprising at least two networks, and

10 (b) identifying correlative changes in at least two value sets between said two or more data integration maps with said different conditions, wherein said correlative changes predict a behavior of said biochemical system.

2. The method of claim 1, wherein said biochemical system is selected from the group consisting 15 of a cell, tissue and organism, or a constituent system thereof.

3. The method of claim 1, wherein said value sets further comprise at least two or more data elements.

4. The method of claim 1, wherein said value 20 sets further comprise at least one value set having three or more data elements.

5. The method of claim 1, wherein said value sets further comprise a data element corresponding to a physical interaction.

25 6. The method of claim 1, wherein said at least two or more networks further comprise three or more networks.

7. The method of claim 1, wherein said two or more data integration maps further comprise a data integration map having two or more perturbed conditions.

8. The method of claim 1, wherein said two or
5 more data integration maps further comprise a data integration map having perturbed conditions for substantially all components within at least one of said networks.

9. The method of claim 1, wherein said
10 correlative changes in at least two value sets between said two or more data integration maps further comprise value sets within the same network.

10. The method of claim 1, wherein said
correlative changes in at least two value sets between
15 said two or more data integration maps further comprise value sets within different networks.

11. The method of claim 1, wherein said
correlative changes in at least two value sets between
said two or more data integration maps further comprise
20 changes in three or more value sets.

12. The method of claim 1, wherein said
correlative changes in at least two value sets between
said two or more data integration maps further comprise
jointly coordinated or inversely coordinated changes in
25 data elements.

13. The method of claim 1, wherein said correlative changes in at least two value sets between said two or more data integration maps further comprise data elements selected from the group consisting of
5 nucleic acid expression, protein expression, polypeptide-polypeptide interaction, nucleic acid-polypeptide interaction, metabolite abundance, and growth rate.

14. The method of claim 1, wherein said at
10 least two networks further comprise at least five components for each of said networks.

15. The method of claim 1, wherein said behavior is selected from the group consisting of cellular phenotype, biochemical activity, expression level and
15 accumulation level.

16. A method of predicting a behavior of a biochemical system, comprising:

(a) obtaining a first data integration map of a biochemical system, said data integration map comprising
20 value sets of two or more data elements for at least two networks;

(b) producing a second data integration map of said biochemical system under a perturbed condition, said second data integration map comprising said value sets of
25 two or more data elements for said at least two networks, and

(c) identifying correlative changes in at least two value sets in said second data integration map with
said perturbed condition, wherein said correlative changes
30 predict a behavior of said biochemical system.

17. The method of claim 16, wherein said biochemical system is selected from the group consisting of a cell, tissue and organism, or a constituent system thereof.

5 18. The method of claim 16, further comprising at least one value set having three or more data elements.

19. The method of claim 16, wherein said value sets of two or more data elements further comprise three or more data elements.

10 20. The method of claim 16, wherein one of said data elements is a physical interaction.

21. The method of claim 16, wherein said at least two or more networks further comprise three or more networks.

15 22. The method of claim 16, wherein said second data integration map further comprises two or more perturbed conditions.

20 23. The method of claim 16, wherein said second data integration map further comprises perturbed conditions for substantially all components within at least one of said networks.

25 24. The method of claim 16, wherein said correlative changes in at least two value sets within said second data integration map further comprise value sets within the same network.

25. The method of claim 16, wherein said correlative changes in at least two value sets within said second data integration map further comprise value sets within different networks.

5 26. The method of claim 16, wherein said correlative changes in at least two value sets within said second data integration map further comprise changes in three or more value sets.

10 27. The method of claim 16, wherein said correlative changes in at least two value sets within said second data integration map further comprise jointly coordinated or inversely coordinated changes in data elements.

15 28. The method of claim 16, wherein said correlative changes in at least two value sets within said second data integration map further comprise data elements selected from the group consisting of nucleic acid expression, protein expression, polypeptide-polypeptide interaction, nucleic acid-polypeptide interaction,
20 metabolite abundance, and growth rate.

29. The method of claim 16, wherein said at least two networks further comprise at least five components for each of said networks.

30. The method of claim 16, further comprising
25 repeating steps (b) and (c) at least once.

31. The method of claim 16, wherein said behavior is selected from the group consisting of cellular phenotype, biochemical activity, expression level and accumulation level.

5 32. A method of predicting a behavior of a biochemical system, comprising:

(a) obtaining a first physical interaction map of a biochemical system, said physical interaction map comprising value sets of a physical interaction data element and an expression data element for at least two independent networks;

10 (b) producing a second physical interaction map of said biochemical system under a perturbed condition, said second physical interaction map comprising said value sets of a physical interaction data element and an expression data element for at least two independent networks, and

15 (c) identifying correlative changes in at least two value sets in different independent networks in said second physical interaction map with said perturbed condition, wherein said correlative changes predict a behavior of said biochemical system.

20 33. The method of claim 32, wherein said biochemical system is selected from the group consisting of a cell, tissue and organism, or a constituent system thereof.

25 34. The method of claim 32, wherein said expression data element further comprises a nucleic acid expression data element and a polypeptide expression data element.

35. The method of claim 32, wherein said at least two or more independent networks further comprise three or more independent networks.

36. The method of claim 32, wherein said second physical interaction map further comprises two or more perturbed conditions.

37. The method of claim 32, wherein said second physical interaction map further comprises perturbed conditions for substantially all components within at least one of said independent networks.

38. The method of claim 32, wherein said correlative changes in at least two value sets in different independent networks in said second physical interaction map further comprise changes in three or more value sets.

39. The method of claim 32, wherein said correlative changes in at least two value sets in different independent networks in said second physical interaction map further comprise jointly coordinated or inversely coordinated changes in said data elements.

40. The method of claim 32, wherein said correlative changes in at least two value sets in different independent networks in said second physical interaction map further comprise data elements selected from the group consisting of nucleic acid expression, protein expression, polypeptide-polypeptide interaction, nucleic acid-polypeptide interaction, metabolite abundance, and growth rate.

41. The method of claim 32, wherein said at least two independent networks further comprise at least five components for each of said independent networks.

42. The method of claim 32, further comprising
5 repeating steps (b) and (c) at least once.

43. The method of claim 32, wherein said behavior is selected from the group consisting of cellular phenotype, biochemical activity, expression level and accumulation level.

10 44. A method of identifying functionally interactive components of a biochemical system, comprising:

- (a) obtaining a set of components within a biochemical system linked by physical interactions;
- 15 (b) obtaining a set of components within a biochemical system linked by expression or activity, and
 - (c) integrating the set of physically linked components with the set of components linked by expression or activity to produce a network of common components
- 20 functionally interactive within the system, each component within said network of common components being characterized as having at least one physical interaction with a component within said set of components linked by expression or activity.

45. The method of claim 44, wherein said physical interactions further comprise polypeptide-polypeptide interactions, polypeptide-nucleic acid interactions and nucleic acid-nucleic acid interactions.

46. The method of claim 44, wherein said expression further comprises transcription or translation.

47. The method of claim 44, wherein said network further comprises two or more pathways.

10 48. The method of claim 44, wherein said network further comprises a biochemical pathway, a gene expression pathway and a regulatory pathway.

49. A method of identifying a component of a biochemical network, comprising:

15 (a) preparing a physical interaction map between two or more system components;

(b) identifying a system component exhibiting altered expression or activity in response to perturbation of a pathway component, and

20 (c) refining the physical interaction map to include a pathway component, an altered system component and an unaltered system component exhibiting at least one physical interaction with an altered system component, said refinement identifying at least one component of an biochemical interaction network by inclusion into said 25 physical interaction map.

50. The method of claim 49, wherein said component further comprises nucleic acid or polypeptide.

51. The method of claim 49, wherein said biochemical network further comprises two or more
5 pathways.

52. The method of claim 49, wherein said biochemical network further comprises a biochemical pathway, a gene expression pathway, and a regulatory pathway.

10 53. The method of claim 49, wherein said physical interaction map further comprises polypeptide-polypeptide interactions, polypeptide-nucleic acid interactions and nucleic acid-nucleic acid interactions.

15 54. The method of claim 49, further comprising perturbing two or more pathway components.

55. The method of claim 49, further comprising perturbing five or more pathway components.

20 56. The method of claim 49, wherein said altered expression further comprises altered transcription or translation.

57. A method of identifying a component of a biochemical network, comprising:

(a) perturbing the expression or activity of at least one pathway component;

5 (b) measuring a response of one or more pathway components;

(c) determining physical interactions between one or more system components and said one or more pathway components to identify candidate network components, and

10 (d) determining a change in expression or activity of a candidate network component affected by the perturbation of at least one pathway component, wherein a candidate network component exhibiting a change in expression or activity is identified as a component of the

15 biochemical network.

58. The method of claim 57, wherein said component further comprises nucleic acid or polypeptide.

59. The method of claim 57, wherein said biochemical network further comprises two or more pathways.

60. The method of claim 57, wherein said biochemical network further comprises a biochemical pathway, a gene expression pathway, and a regulatory pathway.

25 61. The method of claim 57, further comprising perturbing two or more pathway components.

62. The method of claim 57, further comprising perturbing five or more pathway components.

63. The method of claim 57, wherein said change in expression further comprises a change in transcription
5 or translation of said candidate network component.

64. A method of screening for compounds that restore a perturbation state of a biochemical system, comprising:

- (a) obtaining a data integration map of a perturbed biochemical system, said data integration map comprising at least two networks;
- (b) contacting a biochemical system exhibiting a perturbation state corresponding to said data integration map with a test compound, and
- 15 (c) producing a second data integration map of said biochemical system contacted with said test compound, a compound that restores perturbed states in at least two value sets of said data integration map to unperturbed states indicating that said compound has biochemical system restoring activity.

65. The method of claim 64, wherein said biochemical system is selected from the group consisting of a cell, tissue and organism, or a constituent system thereof.

25 66. The method of claim 64, wherein said data integration map of a perturbed biochemical system, further comprises two or more perturbed conditions.

67. The method of claim 64, wherein said at least two or more networks further comprise three or more networks.

68. A method of diagnosing or prognosing a pathological condition, comprising:

- (a) comparing a data integration map of a biochemical system for an individual suspected of having a pathological condition to one or more data integration maps of said biochemical system produced from an individual exhibiting a known condition, said data integration maps comprising at least two networks, and
- (b) identifying a data integration map representing said known condition that is substantially the same as said data integration map for said individual suspected of having a pathological condition, said identified data integration map indicating the presence or absence of a pathological condition.

69. The method of claim 68, wherein said biochemical system further comprises a cell, a tissue, or a constituent system thereof.

70. The method of claim 68, wherein said data integration map of said biochemical system, further comprises two or more perturbed conditions.

71. The method of claim 68, wherein said at least two or more networks further comprise three or more networks.

72. The method of claim 68, wherein said known condition further comprises a normal or pathological condition.

73. The method of claim 68, wherein said known
5 condition further comprises one or more prognostic conditions.

74. The method of claim 68, wherein said known condition further comprises one or more predisposition conditions.

RECEIVED
U.S. PATENT AND TRADEMARK OFFICE
JULY 1978